

**REMARKS**

Claims 1, 3-6 and 22-24 are all the claims pending in the application. Claims 2, 7-21 and 25-36 have been canceled.

Claims 22-24 have been placed in independent form. Accordingly, these amendments are formal in nature, and do not in any way limit the scope of equivalents. Also, no new matter is added.

**A) Claim Rejections - 35 U.S.C. § 102(b)**

Claims 1 and 3-5 were rejected under 35 U.S.C. § 102(b) as being anticipated by Makuuchi, *et al.* (U.S. Patent No. 6,117,815).

According to the Examiner the Makuuchi *et al.* patent discloses a process wherein sodium alginate in the form of either an aqueous solution or a powder is exposed to either gamma-ray radiation or electron beam radiation at a dose of 10-500 kGy, whereupon the sodium alginate is decomposed to produce a low-molecular weight polysaccharide. The Examiner asserted that the dosage disclosed in the Makuuchi *et al.* patent complies with the dosage satisfied by the formula set forth in the instant Claims 1, 3, and 4 and the sodium alginate is a glycosaminoglycan as required by Claim 5. The Examiner further advised that the formula per say in Claim 1 was given no weight because the formula does not clearly establish the dosage of electron beam used in the claimed process.

This rejection is traversed, respectfully, because the Makuuchi *et al.* patent does not teach each and every element of the claimed invention.

The present invention is a process for producing a predetermined or controlled lower molecular weight saccharide. Further, the present Claim 1 specifically recites that the polysaccharide for which the molecular weight is lowered is 5,000 to 70,000 Da. In contrast, the Makuuchi *et al.* patent does not teach or disclose any way to control or predetermine the lower molecular weight. Further, the sodium alginate of Makuuchi *et al.* has a molecular weight of about 420,000 (column 2, lines 22-23), way above that of the weight average molecular weight of the polysaccharide fraction used in the process of the claims.

In addition, the Examiner's reason for ignoring the formula in Claim 1 is technically flawed. The Examiner appears to be saying that the formula has been ignored because the strength of the electron beam is not specified. However, once one of ordinary skill in the art selects a weight average molecular weight of the saccharide having a lowered molecular weight, the dosage becomes specified. That is, the equation does not accommodate any electron beam dosage. Rather, it accommodates only those dosages that will give the desired weight average molecular weight of the saccharide having a lowered molecular weight from the polysaccharide having a weight average molecular weight of 5, 000 to 70,000 Da.

Accordingly, the Makuuchi *et al.* patent does not teach any of the required elements of the present Claim 1.

In view of the above remarks, the Examiner is requested, respectfully, to reconsider and remove the rejection.

**B) Claim Rejections - 35 U.S.C. § 103(a)**

Claims 1, 3-6 and 21-24 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Makuuchi, *et al.* (U.S. Patent No. 6,117,815) in view of De Ambrosi, *et al.* (U.S. Patent No. 4,987,222).

With respect to Claims 1 and 3-6, the Examiner asserted that the Makuuchi *et al.* patent teaches every element of the claims except for the specific glycosaminoglycans recited in Claim 6, namely hyaluronic acid, chondroitin sulphate, dermatan sulphate, keratan sulphate, heparin sulphate, and heparan. In order to compensate for this deficiency, the Examiner cited De Ambrosi *et al.* as teaching the equivalence of sodium alginate and other glycosaminoglycans such as heparin, herparan sulphate, dermatan sulphate, keratan sulphate, and hyaluronic acid. Column 1, lines 14-20. The Examiner further asserted that De Ambrosi *et al.* teaches the equivalence of these glycosamindoglycans for application of gamma-ray radiation in order to lower the average molecular weight of the irradiated glycosaminoglycan.

With respect to Claims 21-24, the Examiner asserted that Makuuchi *et al.* teach all of the limitations of the claims except irradiating hyaluronic acid. However, in order to compensate for this deficiency, the Examiner relied on De Ambrosi *et al.* as teaching the equivalence of sodium alginate and hyaluronic acid for purposes of lowering the molecular weight via gamma-ray radiation.

The Examiner further recognized that the De Ambrosi *et al.* patent does not teach the equivalence of gamma-ray radiation and radiation with an electron beam. However, the

Examiner asserted that Makuuchi *et al.* teaches that radiation with an electron beam and gamma-ray radiation is equivalent.

For the following reasons, the rejection is traversed, respectfully.

As to Claims 1 and 3-6, the De Ambrosi *et al.* patent does not in anyway make up for the deficiencies of the Makuuchi *et al.* patent with respect to the elements of the present Claim 1. Accordingly, even if the teachings of the two references were combined, the present invention would not be achieved.

Regarding claims 22-24, radiation with an electron beam is very different in the dose rate from gamma-ray radiation ( $10^{11}$  times larger in dose per second). Thus radiation with an electron beam can lower the molecular weight in a short time. On the other hand, when the molecular weight is lowered by using gamma-ray radiation, radiation for a long time is required. Therefore, for gamma-ray radiation, the interval described at col. 3, line 12 in De Ambrosi *et al.* is required. Thus, contrary to the Examiner's assertion, radiation with an electron beam is not equivalent to radiation with gamma-rays.

Also, according to De Ambrosi *et al.*, glucosaminoglycans, such as heparan sulphate, dermatan sulphate, chondroitin-4-sulphate, chondroitin-6-sulphate, hyaluronic acid and alginic acid, having a molecular weight of 1000 to 35,000 daltons in the solid state or in solution form are obtained with gamma-ray radiation of 2.5 to 20 Mrad (25 to 100 kGy). However, De Ambrosi *et al.* neither discloses nor suggests the specific relationship recited in claims 22-24, in which a hyaluronic acid fraction having a molecular weight of 600 to 1200 kDa in a liquid state is irradiated with an electron beam of 10-30, 30-50 or 50-80 kGy to obtain a lowered hyaluronic

acid having a molecular weight of 2500 to 4000, 1700 to 2500 or 1300 to 1700 Da, respectively.

Therefore, the method of claims 22-24 is not taught or suggested by the combination of the cited references.

Accordingly, the Examiner is requested, respectfully, to reconsider and remove this rejection.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

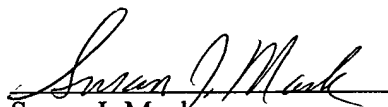
Respectfully submitted,

SUGHRUE MION, PLLC  
Telephone: (202) 293-7060  
Facsimile: (202) 293-7860

WASHINGTON OFFICE

**23373**

CUSTOMER NUMBER

  
Susan J. Mack  
Registration No. 30,951

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